Zero-Calorie Sweeteners May Trigger Blood Sugar Risk By Screwing With Gut Bacteria

Artificial sweeteners don't have calories – so why are these mice getting fat?

(Cornucopia – The Verge – Arielle Duhaime-Ross) When artificial sweeteners are in the news, it's rarely positive. In the last few years, sweeteners have been linked to everything from Type 2 diabetes to cardiovascular disease, high blood pressure, and stroke. Still, products like Splenda and Sweet'N Low remain a cornerstone of many a weight-loss strategy, mostly because doctors don't quite understand how sweeteners contribute to disease. That may soon change, however, as results from a study, published today in *Nature*, point to a possible mechanism behind these adverse health effects.

"Our results suggest that in a subset of individuals, artificial sweeteners may affect the composition and function of the gut microbiome" in a way that would lead to high blood-sugar levels, said Eran Elinav, an immunologist at the Weizmann Institute of Health in Israel and a co-author of the study, during a press conference yesterday. This, the researchers say, is bad for human health because when sugar levels are high in the blood, the body can't break it down, so it ends up being stored as fat.

To reach these conclusions, Elinav and his team first tested the effect of three common artificial sweeteners – aspartame, sucralose, saccharin – on rodents. They found that each of the sweeteners induced a change in blood sugar levels that surpassed that of the mice who consumed actual sugar. And later tests involving the main sweetening agent in Sweet'N

Low, saccharin, yielded similar results in both lean and obese mice.

But mammals don't actually digest artificial sweeteners – that's why they're "calorie-free" – so the reasons why these mice were experiencing blood-glucose alterations was still mysterious, Elinav said. Still, the researchers had an idea: maybe the bacteria that lived in the guts of the mice were interacting with the sweeteners.

So the researchers performed several experiments to test their idea. In one, they gave antibiotics to mice who had been fed sweeteners regularly. Antibiotics kill gut bacteria, and when these mice had their microbial guests cleaned out, their blood sugar levels went back to normal. In another experiment, the scientists transplanted feces – a rich source of gut microbes – from sweetener-fed mice into rodents that had never consumed artificial sweeteners. The procedure caused the recipient mice to experience oddly high blood glucose, like the mice in the sweetener group. Finally, Elinav and his colleagues used genetic analysis to reveal that alterations in the composition of microbial colonies were also accompanied by changes in bacterial function – changes that could very well explain why the mice were experiencing such high blood sugar.

But findings in mice aren't nearly as convincing as findings in people, so the researchers set out to investigate human sweetener consumption. In the first experiment, the researchers analyzed the blood-sugar levels and gut bacteria colonies of 381 participants. And, as expected, Elinav and his colleagues found that people who consumed sweeteners in large quantities also showed disturbances in several metabolic parameters – including increased weight – as well as distinct microbial changes in their guts.

The results from the second, much smaller human experiment might actually be the most illuminating.

“We followed for a single week a group of seven human volunteers who do not consume sweeteners as part of their normal diet,” Elinav said. During that period, the researchers gave them a single dose of saccharin, and monitored their vitals. After just four days, half the participants showed microbial alterations and increases in blood sugar levels, he explained, “while the other subset had no meaningful effect immediately following the consumption of sweeteners.”

In other words: some people are more susceptible to the effects of artificial sweetener than others.

A causal link

The handful of studies suggest that consuming non-caloric artificial sweeteners boosts the risk glucose intolerance in both humans and mice, as a result of changes in gut microbe function, the researchers wrote in their report. Yet, because of the preliminary nature of their results and the small number of human participants involved, they stopped short of suggesting that people change their eating habits. “By no means are we prepared to make recommendations as to the use and dosage of artificial sweeteners based on the results of this study,” said Eran Segal, a study co-author also at the Weizmann Institute of Health.

Other researchers, however, were more forthcoming.

“People need to be much more mindful of what they are eating and drinking and make efforts to avoid products that have added sweeteners in any form” said Susan Swithers, a behavioral neuroscientist at Purdue University who wasn’t part of the *Nature* study, in an email to *The Verge*. The studies showed not only a causal link between the changes in the gut and artificial sweeteners, but that the observed changes happen quickly, she wrote.

Not everyone agrees with the design the researchers used to address the question about artificial sweeteners and weight

gain. Christopher Gardner, a food scientist at Stanford University who didn't participate in the study, says that the fact that the researchers gave the FDA's maximal acceptable daily intake of saccharin to the human participants – about 5 mg / kg body weight per day – isn't ideal. In a real-life setting, that dose would be the equivalent to a 150-pound person consuming 42 12-ounce sodas per day, or 8.5 packets of pink Sweet 'n Low per day. "That may be 'acceptable' according to some set of guidelines," Gardner wrote in an email, "but it should be noted that realistically this is a very high dose they are using and one that wouldn't be consumed by a typical consumer."

Still, the idea that we might finally have an explanation for the adverse health effects seen in certain sweetener studies is worth paying attention to. Should the findings prove reproducible, doctors will be tasked with understanding why some people are susceptible to microbiome alterations, while others aren't. And sweetener companies will have to address the criticism – in addition to rethinking their marketing strategies. "The work is important," Swithers said, "because it underscores the role that artificial sweeteners may play in contributing to the very problems they were designed to help."